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The Scientist to Scientist Colloquium was created by The Keystone Center and a planning committee of distinguished scientists. The goals was, and still is, to bring together leading researchers and other members of the scientific community to share with each other what kind of work they do at the outer reaches of science.

The chairman of the 1992 Scientist to Scientist Colloquium, held August 15-20 in Keystone, Colorado, was Dr. Eric Lander, Member of the Whitehead Institute for Biomedical Research, and the co-chairman was Dr. Ronald Cape, co-founder of Darwin Technologies, Inc.

Seven major topics were addressed over a five-day period, including: Evolution, High Precision Physics, Chemistry, Managing Science: What Works?, Astrophysics, Immunology, and Computer Science. Each major session consisted of a topic chair and two speakers. The summary includes a brief synopsis of each speaker's presentation and an attempt to give a flavor of the discussion that followed.

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FINAL TECHNICAL REPORT

ONR Grant No. N00014-89-J-1030
"1992 Scientist to Scientist Colloquium"

The Keystone Center
Keystone, Colorado

THE KEYSTONE CENTER'S 1992 SCIENTIST TO SCIENTIST COLLOQUIUM

MEETING SUMMARY

August 15 - 20, 1992
Keystone, Colorado

The Keystone Center, founded in 1975, is a national non-profit organization located in the Rocky Mountains at Keystone, Colorado, 75 miles west of Denver. The Center is organized around three major programmatic areas: (1) The Keystone Science and Public Policy Program, which facilitates the resolution of national public policy conflicts through the use of an innovative consensus dialogue approach; (2) The Keystone Science School Program, which provides residential natural science education programs for students of all ages with emphasis on sound scientific understanding of nature and our relationship to the environment; (3) The Symposia on Molecular and Cellular Biology, which offers an annual series of colloquies addressing critical developments in science and research. The Center's programs are funded by grants from foundations, corporations, government, individuals, and in the case of the Science School Program, fees paid by students.

BOARD OF TRUSTEES

PREFACE

For the second consecutive summer, The Keystone Center brought together leading American scientists, from all disciplines, for the Scientist to Scientist Colloquium. Created by The Keystone Center and a planning committee of distinguished scientists from the major fields, the first Colloquium was held in 1991. The goal was, and still is, to bring together leading researchers and other members of the scientific community to share with each other what kind of work they do at the outer reaches of science, why it is so compelling to them, and why others should also be excited as they gain some understanding beyond their own fields. The Keystone Center feels that this kind of interdisciplinary communication is lacking in the scientific community and must be encouraged.

The 1992 Scientist to Scientist Colloquium was held August 15-20 in Keystone, Colorado. The chairman of this year's Steering Committee was **Dr. Eric Lander**, Member of the Whitehead Institute for Biomedical Research, and the co-chair was **Dr. Ronald Cape**, co-founder of Darwin Technologies, Inc. Seven major topics were addressed over a five-day period, including: Evolution, High Precision Physics, Chemistry, Managing Science: What Works?, Astrophysics, Immunology, and Computer Science. In addition to these formal presentations, small, diverse groups were organized by general participants to address other important issues facing the scientific community. "Science Education: What is the Role of the Professional Scientist?," "Women in Science," and "How Should American Scientists and Science Funding Agencies Relate to Japanese Science and Technology Initiative?" are the titles of a few of these discussions.

Each major session consisted of a topic chair, who introduced the subject matter, and two speakers who presently investigate cutting-edge issues or developments in their respective fields. The summary that follows includes a brief synopsis of each speaker's presentation and an attempt to give a flavor of the discussion that followed. The discussions, although not emphasized in the individual summaries, were perhaps the most fruitful facet of the Colloquium. Equal time was given to the participants to ask questions not only about the subject matter of the presentations, but also about attitudes, assumptions, approaches, and concerns that are particular to a field of study. Questions such as, "What is the definition of a cell?" and "Where are we located in the universe?" seemed simple and straightforward, but the discussions that evolved from such questions illuminated the differences that exist between scientific disciplines. The observations of one conferee contained in the enclosed editorial of Bio/Technology may give a more intimate sense of the proceedings of the 1992 Colloquium.

The Keystone Center is grateful for the support given by all funders who made the 1992 Scientist to Scientist Colloquium possible:

The Alfred P. Sloan Foundation
The Department of the Navy, Office of Naval Research
Nature Publishing Company and Bio/Technology Magazine
AT&T Bell Laboratories

Already The Keystone Center is organizing a Scientist to Scientist Colloquium for 1993. We hope to have an event that equals, if not surpasses, our past successes.

Robert W. Craig
President, The Keystone Center

TABLE OF CONTENTS

TABLE OF CONTENTS, cont.

SESSION ONE:

THE EVOLUTION OF FORM AND FUNCTION IN MOLECULES AND ORGANISMS

SPEAKERS:

Dr. Jack W. Szostak
Harvard Medical School/Massachusetts General Hospital

Dr. Rudolf A. Raff
Indiana University

The first session of the 1992 Scientist to Scientist Colloquium was entitled "The Evolution of Form and Function in Molecules and Organisms." The topic chair, **Dr. Ford Doolittle** of Dalhousie University, introduced the participants to the field of evolution by outlining some of the critical concepts that underlie the presentations of the two speakers who followed.

The first speaker was **Dr. Jack Szostak**, a professor of genetics at Harvard Medical School and Massachusetts General Hospital. Dr. Szostak's current work essentially focuses on the origin of life. He is trying to simulate the development of the earliest living cells in his laboratory. He is not looking to create a computer model or a machine, but is trying to create an extremely simple cell that has the ability to replicate and evolve.

Dr. Szostak explained that until ten years ago, molecular biologists knew of no molecule in which both phenotype and genotype were expressed. Such a molecule would contain the essential information needed for replication, evolution, and essentially, life. A monumental breakthrough was the discovery of an RNA molecule that also acted as an enzyme. This breakthrough allowed Dr. Szostak and others to construct theories and run experiments that investigate how this molecule could replicate and evolve.

Dr. Szostak walked the participants through the chemical processes that could transform simple sugars and amino acids into single-stranded and double-stranded RNA molecules. As this process is repeated many times, some random sequences are created that enable an RNA double-stranded molecule to separate and replicate its complement. Dr. Szostak explained that if this RNA is contained within a membrane, it will continue to replicate itself, forming a feedback loop. The RNA molecules that replicate themselves most efficiently, therefore, will have a reproductive and evolutionary advantage. This is the beginning of evolution.

The concept of this development is straightforward relative to figuring out how to reconstruct this process in the lab. Dr. Szostak showed participants how he is attacking the problems of identifying RNA molecules that have the ability to replicate, how these molecules are isolated, and how he is introducing mutations and isolating ever more efficient replicators.

The discussion that followed the presentation touched on two main questions. What is the nature of the dividing line between what is life and evolution and what is merely chemistry? Also, does the single genetic code present today indicate that all living cells evolved from a single ancestor? The discussion not only clarified the subject matter, but also clearly demonstrated that scientists from different fields work with different sets of assumptions. At the beginning of the presentation, "evolution" meant something very different to the physicists and chemists than it did to the biologists. Dr. Szostak's clarifications and explanations showed that while these disciplinary differences in assumptions and terminology can be confusing, they are certainly not a significant barrier to communication and understanding.

The second half of the evolution session was led by **Dr. Rudolf Raff**, Director of the Institute for Molecular and Cellular Biology and Professor of Biology at Indiana University. Dr. Raff's presentation delved into the questions concerning how an organism develops from a fertilized egg into an adult, and specifically how body plans are created and molded.

A body plan, Dr. Raff explained, is a blueprint for a group of organisms. It is a sketch of the major structures and relationships between structures that exist within an organism. Animals that have similar body plans have been separated by taxonomists into 33 different phyla. An example of one of these body plans, the planarians, was described by Dr. Raff. All the organisms within this phylum have three cell layers, bilateral symmetry, an identifiable end, and a nervous system that runs down the body axis.

In his presentation, Dr. Raff showed that animal body plans began to appear very quickly at the beginning of the Cambrian period, roughly 550 million years ago. Since that time, no new body plans have appeared. One explanation is that the availability of empty ecological niches restricts survival of new body plans. Dr. Raff pointed out, however, that about 275 million years ago 95 percent of the species went extinct, leaving many niches unfilled. And yet no new body plans developed. This has provided evidence that the restriction on the evolution of new body plans is developmental.

At first glance, it would seem that the eggs of different organisms are very similar and that as they develop into adults, their morphological similarities would gradually decrease. Contrary to this fan-like vision of development, the reality seems to be an hourglass procession of development from egg to adult. There is a diversity in the early developmental modes and early on there is a certain amount of freedom to evolve. At some midpoint, however, there is an evolutionary constrained pattern of development and the evolution of many organisms seems to converge. Later in development, organisms are again free to evolve and the similarities noticed at the bottleneck slowly disappear.

Although much is still unknown about the mechanisms that control these processes, Dr. Raff feels that he is beginning to answer some basic questions. His experiments indicate that a global information system probably controls early embryonic development. Later in the development of the embryo, evolution seems to work in domains within the embryo, which have been partitioned and insulated from other areas. The counter-intuitive middle stage of development, at the narrow neck of the hourglass, is especially intriguing. At this stage evolution and development apparently act at both levels. The same information seems to be directing events at both the global and specific levels, in a highly interactive way.

Many of the participants were intrigued by the mystery of the lack of new body plans. To many it seemed as though evolution has been frozen. The resulting discussion revolved around how this could have happened. Dr. Raff explained that once he and his co-workers more fully understand the processes of development and what exactly is happening, this will ultimately lead to discovering the mechanisms controlling this development and lead closer to the answers to the participants' questions.

SESSION TWO:

HIGH PRECISION PHYSICS

SPEAKERS:

Dr. William D. Phillips
National Institute of Standards and Technology

Dr. Clifford M. Will
Washington University

APPENDIX C:

1992 COLLOQUIUM STEERING COMMITTEE MEMBERS

1992 KEYSTONE SCIENTIST TO SCIENTIST COLLOQUIUM
PROJECT STEERING COMMITTEE

Chairman:

Dr. Eric S. Lander
Member
The Whitehead Institute for Biomedical Research

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California Institute of Technology

Dr. Gilbert S. Omenn
Dean, School of Public Health/Community Medicine
University of Washington

APPENDIX D:

EDITORIAL ON THE 1992 SCIENTIST TO SCIENTIST COLLOQUIUM FROM THE OCTOBER 1992 ISSUE OF BIO/TECHNOLOGY MAGAZINE

FIRST WORD/

LIGHT AND VERITY

By Douglas McCormick

There was a hint of the biblical—light and the beginnings of things—about the Keystone Center's Scientist to Scientist meeting, an August gathering of some seventy august American scientists.

Ron Cape (ex-Cetus, ex-Chiron, and now starting a new company called Darwin Molecular Technologies) and the non-profit Keystone Center started the conference a year ago to do something that other august groups—from the National Academy to the faculties of big research universities—do not: bring together first-rate scientists from many disciplines to learn what is happening on the frontiers of fields far removed from their own.

Written words—and only a few hundred of them, at that—can scarcely convey the resulting excitement. Remember when the doors of science first opened for you, when you first peered inside and saw the...well, grandeur? Remember when the new concepts and new insights seeped into your very dreams and transformed the way you looked at the waking world?

At its best, that's what Keystone was like—six different versions of the very best introductory science course you ever had (David Baltimore, Irving Weissman, and Leroy Hood taught introductory immunology), delivered to a roomful of students mostly unfamiliar with the material, but eager, intelligent, critical (in the most constructive sense), and questioning.

Let There Be Light

And so it went for six days, often from eight in the morning to after ten at night.

Cosmologists peered back in time toward the great wall, tracking photons almost to the instant they first condensed out of the blazing primordial cloud to produce the very lumpy universe we now see around us.

Biophysicists traced the picosecond pulses of chlorophyll's astounding network of molecular antennae, as they trap light and funnel its fire into the maw of the chloroplast's reaction center for conversion into living energy.

Quantum physicists brought time almost to a standstill, making "optical molasses"—and the world's most precise clocks— from finely tuned laser light, a honey trap that slows atoms to crawl, cooling them to within a few thousandths of a degree of absolute zero.

Evolutionary biologists squinted back some three billion years to the beginnings of life on earth—perhaps as fortuitous tangles of self-replicating RNA captured, two by two, in natural liposome, combining and redividing in some gently lapping Precambrian surf.

Computer scientists, too, acknowledged the power of the "evolutionary method," as they described arthropoid robots that walk and stalk, and computer programs that manage their own evolution to produce rock videos and super-efficient sorting algorithms.

Questions

It was a time for asking the stupid questions and musing on the big ones. A geophysicist could ask, relatively unselfconsciously, "What is a cell?" A Nobel laureate physician could ask, "What is time?"

A prominent biologist could aver, "Evolution stopped when humanity invented medicine, but before too long, we will be altering ourselves intentionally. It will happen."

"Or perhaps," an artificial-intelligence guru could retort, "this will be the age in which the evolution of electronic life succeeds the evolution of chemical life."

Perhaps.

Amidst this meeting's melding of Darwinian method and the majesty of creation, though, ran the subtext of a verse from Genesis:

> Now the whole earth had one language and few words. And as men migrated... they said to one another... "Come, let us build ourselves a city, and a tower with its top in the heavens, and let us make a name for ourselves, lest we be scattered abroad upon the face of the whole earth."
>
> And the Lord came down to see the city and the tower, which the sons of men had built. And the Lord said, "Behold, they are one people, and they have all one language; and this is only the beginning of what they will do; and nothing that they propose to do will now be impossible for them. Come, let us go down, and there confuse their language, that they may not understand one another's speech." So the Lord scattered them abroad from there over the face of all the earth, and they left off building the city.

For a long time, it seemed that the edifice of Western science—humanity's most profound and beautiful artistic achievement, whatever else it may be—was doomed to become a self-limiting Babel of isolated disciplines scattered abroad over the face of the earth, each cut off from the others by its own parochial obsessions and impenetrable jargon. Impious as it may be, we still yearn to build those towers with their tops in heaven, spires not of stone and mortar but of understanding. And the purpose of meetings like Keystone's is to teach us each the other's tongue, so that all can share in the execution and the plan.

The point of all this is synthesis and synergy—the very recipe that created and sustains biotechnology, among other things. We have said before that biotechnology is about the crossing of boundaries—disciplinary, national, species, it doesn't matter. Well, it seems that this may have been too narrow a view. After a week of talking with computer scientists taking lessons from biology, and biologists learning from the physicists how to look even more closely at fundamental life processes, and on and on in a web of new insights and ideas... For a moment, it seemed that all boundaries were in jeopardy—that truly nothing they proposed to do would be impossible to them.

Final Technical Report
August, 1992

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